

1. (Original) A net for supporting one or more cell constructs in the culture chamber of a bioreactor, comprising an array of impermeable pyramidal elements protruding from the face of said net, wherein each of the corners of the base of each of said impermeable pyramidal elements comprises a circular opening.

2. (Currently amended) The net according to claim 1, wherein the diameter of said circular opening is preferably between 0.1mm to 3mm, ~~and more~~ preferably, 1.25mm.

3. (Currently amended) The net according to claim 1, wherein the distance between any two adjacent circular openings situated orthogonally to one another along the x- or y-axis is preferably between 1mm to 10mm, ~~and more~~ preferably, 3mm.

4. (Currently amended) The net according to claim 1, wherein the angle of the outer edges of the pyramidal elements ~~is~~ ~~are~~ preferably between 1° to 179°, ~~and more preferably, 60°~~.

5. (Currently amended) The net according to claim 1, wherein said net is ~~said net is~~ ~~nets may be~~ preferably constructed from a material selected from the group consisting of poly(methyl methacrylate) Plexiglas™, polycarbonate or any solid transparent material.

6. (Currently amended) A bioreactor comprising an inlet half having an opening at one end and an inlet aperture at its opposite end, and an outlet half having an opening at one end and an outlet aperture at its opposite end, wherein said halves are joined at their opening ends such that the hollow interior of said bioreactor forms a culture chamber, and

further comprising at least one net for supporting one or more cell constructs in the culture chamber of a bioreactor, comprising an array of impermeable pyramidal elements protruding from the face of said net, wherein each of the corners of the base of each of said impermeable pyramidal elements comprises a circular opening, wherein said net is positioned transversely within said culture chamber ~~at a predetermined distance from said inlet aperture.~~

7. (Original) The bioreactor according to claim 6, wherein said culture chamber is cylindrical in shape.

8. (Currently amended) The bioreactor according to claim 7, wherein said net is substantially circular.

9. (Currently amended) The bioreactor according to claim 7, wherein the diameter of said net is substantially equal to the diameter of said culture chamber.

10. (Currently amended) The bioreactor according to claim 6, wherein two substantially identical said nets are positioned transversely within said culture chamber ~~at a predetermined distance from each other.~~

11. (Original) The bioreactor according to claim 10, wherein at least one of said nets is permanently affixed to the circumference of said culture chamber.

12. (Original) The bioreactor according to claim 10, comprising means for removably affixing at least one of said nets within said culture chamber.

13. (Original) The bioreactor according to

claim 12, wherein said means comprises a projection which protrudes inward from the circumference of said culture chamber wall.

14. (Original) The bioreactor according to claim 6, wherein said inlet aperture is threaded for suitably attaching means for transferring a fluid medium to said culture chamber.

15. (Original) The bioreactor according to claim 6, wherein said outlet aperture is suitably threaded for attaching means for transferring fluid medium from said culture chamber.

16. (Currently Amended) The bioreactor according to claim 14, wherein said means comprise suitable transfer tubing.

17. (Currently Amended) The bioreactor according to claim 6, wherein said inlet half and said outlet half are joined to each other via suitable means such as screws or bolts.

18. (Currently Amended) The bioreactor according to claim 6, wherein the suitable means for sealing said inlet half with said outlet half comprises an O-ring.

19. (Original) The bioreactor according to claim 6, wherein a fluid distributor mesh is positioned in said inlet half between said inlet aperture and said net.

20. (Original) The bioreactor according to claim 19, wherein a fluid distributor mesh is positioned in said outlet half between said outlet aperture and said net.

21. (Currently Amended) The bioreactor according to claim 20, wherein any of said fluid distributor meshes comprise comprises pores whose diameter is preferably up to 10mm, and more preferably 2mm.

22. (Previously presented) The bioreactor according to claim 6, wherein said bioreactor may be used for bioproduction of therapeutic protein.

23. (Previously presented) The bioreactor according to claim 6, wherein said bioreactor may be used for stem cell expansion.

24. (Currently amended) A bioreactor system comprising:

a. a bioreactor comprising an inlet half having an opening at one end and an inlet aperture at its opposite end, and an outlet half having an opening at one end and an outlet aperture at its opposite end, wherein said halves are joined at their opening ends such that the hollow interior of said bioreactor forms a culture chamber, and comprising two substantially identical nets for supporting at least one cell construct in said chamber, wherein the distance between said nets is substantially equal to the thickness of said at least one cell construct, wherein each of said nets comprises an array of pyramidal elements protruding from the face of said net, wherein the vertex of each of said pyramidal elements comprises a circular opening;

b. a culture medium reservoir for storing a supply of a fluid culture medium, comprising a medium inlet and outlet, and further comprising a gas inlet and outlet;

c. a gas supply for supplying gas to said

medium contained in said reservoir,

d. a heat exchanger for maintaining the temperature of said medium at a constant value, and

e. a pump for pumping said medium from said reservoir into said bioreactor and back to said reservoir.

25. (Original) The bioreactor system according to claim 24, wherein said reservoir comprises a medium sample collection outlet.

26. (Original) The bioreactor system according to claim 24, wherein said pump is a peristaltic pump.

27. (Currently amended) A method for the cultivation of 3-D cell constructs, comprising the following steps:

a. providing a bioreactor system comprising  
i. a bioreactor, said bioreactor comprising an inlet half having an opening at one end and an inlet aperture at its opposite end, and an outlet half having an opening at one end and an outlet aperture at its opposite end, wherein said halves are joined at their opening ends such that the hollow interior of said bioreactor forms a culture chamber, and comprising two substantially identical nets for supporting at least one cell construct in said chamber, wherein the distance between said nets is substantially equal to the thickness of said at least one cell construct, wherein each of said nets comprises an array of pyramidal elements protruding from the face of said net, wherein the vertex of each of said

pyramidal elements comprises a circular opening;

ii. a culture medium reservoir for storing a supply of a fluid culture medium, comprising a medium inlet and outlet;

iii. a gas supply for supplying gas to said medium contained in said reservoir;

iv. a heat exchanger for maintaining the temperature of said medium at a constant value; and

v. a pump for pumping said medium from said reservoir into said bioreactor and back to said reservoir;

b. placing at least one cell construct within said culture chamber, between said nets;

c. pumping said medium from said reservoir into said culture chamber, thereby causing medium perfusion into said cell construct for a suitable period of time; and

d. harvesting the resulting construct.

28. (Currently amended) The method according to claim 27, optionally further comprising:

e. removing a sample of said medium from said reservoir after step c and before step d, in order to determine whether said medium should be replaced with new medium;

f. adding fresh medium to said reservoir when necessary, after optional step e and before step d.

29. (Previously presented) The method according to claim 27, wherein said cell construct consists of a polymeric scaffold seeded with cells.

30. (Original) The method according to claim 29 wherein said polymer is a polysaccharide, preferably alginate.

31. (Previously presented) The method according to claim 29, wherein said cells are human cells, preferably cardiomyocytes.

32. (Previously presented) The method according to claim 27, wherein said 3-D cell constructs are for the bioproduction of therapeutic proteins.

33. (Previously presented) The method according to claim 27, wherein said 3-D cell constructs are for stem cell expansion

34. (New) The net according to claim 2 wherein the diameter of said circular opening is 1.25 mm.

35. (New) The net according to claim 3, wherein the distance between any two adjacent circular openings situated orthogonally to one another along the x- or y-axis is 3 mm.

36. (New) The net according to claim 4, wherein the angle of the outer edges of the pyramidal elements is 60°.

37. (New) The net according to claim 21, wherein any of said fluid distributor meshes comprise pores whose diameter is 2 mm.